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<p>(21) 国際出願番号 PCT/IP99/01224</p> <p>(22) 国際出願日 1999年3月12日(12.03.99)</p> <p>(30) 優先権データ 特願平10/80182 1998年3月12日(12.03.98) JP</p> <p>(71) 出願人 ; および (72) 発明者 輕部征夫(KARUBE, Isao)[JP/JP] 〒216-0002 神奈川県川崎市宮前区東有馬一丁目3番16号 Kanagawa, (JP) 齋藤 敬(SAITOH, Takashi)[JP/JP] 〒116-0013 東京都荒川区西日暮里一丁目42番2-1002号 ライオンズマンション西日暮里第2 Tokyo, (JP)</p> <p>(74) 代理人 弁理士 清水初志, 外(SHIMIZU, Hatsushi et al.) 〒300-0847 茨城県土浦市卸町1-1-1 関鉄つくばビル6階 Ibaraki, (JP)</p>		<p>(81) 指定国 AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, 欧州特許 (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI特許 (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG), ARIPO特許 (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), ユーラシア特許 (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM)</p> <p>添付公開書類 国際調査報告書</p>
<p>(54)Title: APPARATUS FOR AUTOMATICALLY MEASURING MINUTE MEMBRANE POTENTIAL</p> <p>(54)発明の名称 自動微小膜電位計測装置</p> <p>(57) Abstract</p> <p>An apparatus for automatically measuring minute membrane potential, based on a technique developed for controlling a membrane denaturation reaction without using a physical shearing force, for example, a method of causing the destruction of membrane at a limited portion of a living membrane by making a stimulus, such as light and a compound activated by the stimulus react with each other in a membrane, such as a living membrane, this method being applied to a minute electrode to facilitate the insertion thereof into a cell, which has been difficult in the use of a minute metal electrode, and enable membrane potential in a cell to be measured easily, the minute metal electrode enabling the integration thereof and the development of a neural interface in the barrier-free technology.</p> <div style="display: flex; justify-content: space-between; align-items: flex-start;"> <div style="width: 60%;"> <p>A ... STIMULUS</p> <p>1 ... MEMBRANE STRUCTURE</p> <p>2 ... SUPPORT MEMBERS</p> <p>3 ... MEMBRANE DENATURATION REACTION PROMOTING PORTIONS</p> <p>4 ... DENATURED PORTION OF THE MEMBRANE</p> </div> <div style="width: 35%; text-align: right;"> <p>1 膜構造体 2 支持体 3 膜変成反応促進部位 4 膜変成部位</p> </div> </div>		



US006537800B1

(12) **United States Patent**
Karube et al.(10) **Patent No.:** **US 6,537,800 B1**
(45) **Date of Patent:** **Mar. 25, 2003**(54) **APPARATUS FOR AUTOMATICALLY MEASURING MINUTE MEMBRANE POTENTIAL**(75) Inventors: **Isao Karube**, Kanagawa (JP); **Takashi Saitoh**, Tokyo (JP)(73) Assignee: **Center for Advanced Science and Technology Incubation, Ltd.**, Tokyo (JP)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

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(2), (4) Date: **Dec. 28, 2000**(87) PCT Pub. No.: **WO99/46588**PCT Pub. Date: **Sep. 16, 1999**(30) **Foreign Application Priority Data**

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(51) Int. Cl.⁷ **C12M 1/34**(52) U.S. Cl. **435/287.1; 435/285.2; 204/403.13**(58) Field of Search **435/285.2, 287.1; 204/403.13, 403.01, 290.01**(56) **References Cited****PUBLICATIONS**Saito et al. 'Light does and time dependency of photodynamic cell membrane damage.' *Photochemistry and Photobiology*, vol. 68 (1998) No. 5, pp. 745-748.*Robinson, D. A., "The Electrical Properties of Metal Micro-electrodes," *Proceedings of the IEEE*, 56:1065-1071 (1968).Hamill, O. P., et al., "Improved Patch-Clamp Techniques for High-Resolution Current Recording from Cells and Cell-Free Membrane Patches," *Pflügers Archiv*, 391:85-100 (1981).Kurata S., et al., "The Laser Method for Efficient Introduction of Foreign DNA into Cultured Cells," *Experimental Cell Research*, 162:372-378 (1986).Valenzano, D. P., "Photomodification of Biological Membranes with Emphasis on Singlet Oxygen Mechanisms," *Photochemistry and Photobiology*, 46:147-160 (1987).Horn, R., et al., "Muscarinic Activation of Ionic Currents Measured by a New Whole-Cell Recording Method," *J. Gen. Physiol.*, 92:145-159 (1988).Levitani, E. S., et al., "Neuropeptide Modulation of Single Calcium and Potassium Channels Detected with a New Patch Clamp Configuration," *Nature*, 348:545-547 (1990).Bard, A. J., et al., "Chemical Imaging of Surfaces with the Scanning Electrochemical Microscope," *Science*, 254:68-74 (1991).

(List continued on next page.)

Primary Examiner—William H. Beisner(74) *Attorney, Agent, or Firm*—Nixon Peabody LLP(57) **ABSTRACT**

An apparatus for automatically measuring minute membrane potential, based on a technique developed for controlling a membrane denaturation reaction without using a physical shearing force, for example, a method of causing the destruction of membrane at a limited portion of a living membrane by making a stimulus, such as light and a compound activated by the stimulus react with each other in a membrane, such as a living membrane, this method being applied to a minute electrode to facilitate the insertion thereof into a cell, which has been difficult in the use of a minute metal electrode, and enable membrane potential in a cell to be measured easily, the minute metal electrode enabling the integration thereof and the development of a neural interface in the barrier-free technology.

13 Claims, 16 Drawing Sheets